PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/050902	01.03.2005	01.03.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/59, C07C401/00, A61P13/10

Applicant
BIOXELL SPA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Strack, E

Telephone No. +31 70 340-4760

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-15 (partially)

because:

☒ the said international application, or the said claims Nos. 1, 3-5 and 10-15 (see separate sheet) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-9 (partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-5, 10-15
	No:	Claims	6-9
Inventive step (IS)	Yes:	Claims	10-15
	No:	Claims	1-9
Industrial applicability (IA)	Yes:	Claims	2, 6-9
	No:	Claims	1, 3-5 and 10-15 (see separate sheet)

2. Citations and explanations

see separate sheet

Re Item III.

III.1 Claims 1, 3-5 and 10-15 relate to subject-matter considered by this authority to be covered by the provisions of Rule 67.1(iv)PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I)PCT).

III.2 Present claims 1-9 relate to a large number of possible compounds ("vitamin D compound"). Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. The search has therefore been restricted to the compounds of claims 10 and 11 with due regard to the general idea underlying the present invention.

Re Item V.

The applicant's attention is drawn to the fact that the present opinion expressed as to novelty, inventive step and industrial applicability refers only to matter for which an international search report has been drawn up (see section III).

V.1 Article 33(4) PCT

The subject-matter of claims 1, 3-5 and 10-15 involves compositions or substances in a method of treatment of the human/animal body. For the assessment of these claims on the question whether they are industrially applicable, no unitary criteria exist in the PCT Contracting states. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognise the subject-matter of claims related to the use of a compound in medical treatment as industrially applicable. However, the EPO may allow claims related to a known compound in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

V.2 Reference is made to the following document:

D1 : BEERS ET AL: "Merck Manual" 1999, MERCK RESEARCH LABORATORIES, WHITEHOUSE STATION, N.J., XP002340267

D2: MUTSCHLER E: "Arzneimittelwirkungen" 2001, WVG , STUTTGART , XP002340852

V.3 Present claim 6 and 8 are regarded as first medical use claims. The use specified in these claims as they stand now cannot be regarded as a limiting feature. Patents may be obtained for compositions for medical use. However, in the case of a known substance, this can be regarded novel only if the known substance was not previously disclosed for any medical use. Consequently, regardless of which medical use would be specified in these claims, their subject-matter is already anticipated by D2.

V.54 With regard to claims 7 and 9, instructions for use cannot be regarded as a technical feature which would limit the scope of the claim in any way. Therefore, the subject-matter of these claims can also not be regarded as novel with regard to D2.

V.5 Document D1 (page 1893, column 2, paragraph 1-2), which is considered to represent the most relevant state of the art, discloses the treatment of interstitial cystitis with various compounds which are structurally unrelated to Vitamin D. The subject-matter of claims 1 and 3 is therefore novel (Article 33(2) PCT).

Claims 2, 4, 5 and 10-15 are dependent on claim 1 and as such also meet the requirements of the PCT with respect to novelty.

V.6 With regard to the compounds used, pharmacological data in the description are provided only for a limited number of compounds. None of the other variants exemplified or of the innumerable other variants encompassed by the scope of the claims has any technical support in the description. When inventive step is based on the achievement of a technical effect, such as, in this case, the treatment of interstitial cystitis, all the embodiments should exhibit this effect. In other words, it must be credible from the claims that all the claimed alternatives are a solution to the problem posed in the application. However, the number of compounds falling within

the scope of claims 1-5 is such that it is highly unlikely that all of them possess the activity required to achieve the technical effect envisaged. Thus, it is highly likely that part of the subject-matter of these claims does not present the activity claimed, and, consequently, these variants cannot involve an inventive step.

V.7 Inventive Step could be acknowledged for the subject-matter of claims 10-15 if incorporated into a new independent claim. Document D1 (page 1893, column 2, paragraph 1-2) discloses the treatment of interstitial cystitis with various compounds which are structurally unrelated to Vitamin D. The problem to be solved thus appears to be the provision of an alternative treatment for interstitial cystitis. The skilled person would not consider to use the structurally unrelated compounds of claims 10-15 in order to solve the present problem (Article 33(3) PCT).